REMARKS

The Pending Claims

The pending claims are directed to unsymmetrical cyanine dyes incorporating an aza-benzazolium moiety and their method of use for determining the presence of an analyte in a sample. In particular these compounds form fluorescent complexes with nucleic acids and poly(amino acids) and are used to effectively fluorescently stain such molecule.

Claims 1-44 are pending and under acitive consideration. Claims 1-12 and 44 are directed to a method of determining the presence of an analyte in a sample. Claims 13-24 are directed to a to methods for detecting poly(amino acids). Claims 25-43 are directed to methods for detecting nucleic acids.

The Office Action

Claims 1, 13 and 25 are objected to because of informalities.

Claims 1-4, 13 and 14 are rejected under 35 U.S.C. § 102(b) as being anticipated by Haseltine et al. (U.S. Patent 4,003,750).

Claims 1-4, 6, 9, 10, 13-17, 20, 21, 23-25, 38, 39 and 41-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katayose et al. (JP 05-287209).

Claims 5, 11, 22, and 40 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Katayose in view of Mills et al. (U.S. Patent No. 5,221,518).

Claim 12 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Katayose in view of Leushner et al. (U.S. Patent No. 6,083,699).

The Amendment

Claims 1, 13 and 25 are currently amended. Claim 44 is newly added. Claims 1-44 are pending and under active consideration. The claim amendments are fully supported by the specification as originally filed.

Allowable Claims

The Office Action stated that if claims 7 and 8 were presented as independent claims, they would be found allowable. New claim 44 includes the limitations of claims 7 and 8 and is in independent form. Accordingly, it is respectfully submitted that claim 44 is in condition for allowance.

Claim Objections

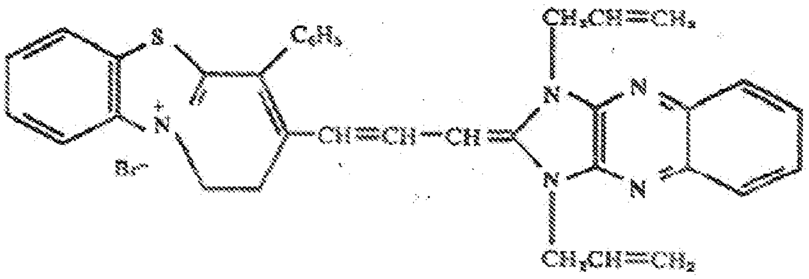
Claims 1, 13, and 25 are objected to because of the use of the word "illiminating" in step (c), which is a misspelling of the intended word, "illuminating". In view of the current amendment correcting this typographical error, Applicant's submit that the claim objections have been rendered moot.

Claim Rejections

Rejection Under 35 U.S.C. § 102(b)

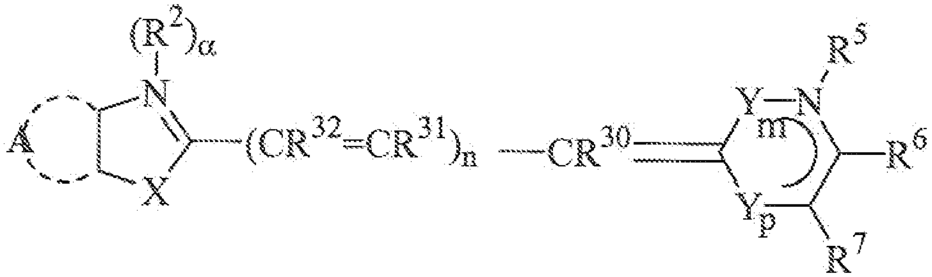
I. Claims 1-4, 13 and 14 are rejected under 35 U.S.C. § 102(b) as being anticipated by Haseltine et al. (U.S. Patent 4,003,750). Applicants respectfully traverse this rejection because: a) the compounds are different, and b) Haseltine does not teach all of the steps of the present claims.

The Office Action identifies Example 3 in Haseltine, which has the following structure:



According to the Office Action, the compound meets the structural limitations recited in Formula I. Based on the following, Applicants respectfully disagree.

The present claims provide a compound of Formula I:



where (in relevant part) R^5 is independently selected from the group consisting of a C_1-C_6 alkyl group, a CYCLIC SUBSTITUENT, TAIL, BRIDGE, -L-Rx and –L-Sc; or R^5 is absent.

Haseltine requires that a fused ring, such as a thiazole in Example 3, be present at positions analogous to R^5 and R^6 in Formula I. The N-fused moiety in Hazeltine appears to be important, as it is present in all examples and embodiments of the invention. The present claims do not permit that sort of substitution at R^5 and R^6.

Furthermore, Haseltine does not even remotely describe the presently claimed method. Haseltine is directed to use of methine dyes for spectral sensitization in photographs. To clarify, a primary step in photography involves excitation of a sensitizing dye that is adsorbed to the surface of a silver halide crystal. West et al. *In The Theory of the Photographic Process*, T. H. James (Ed.), p. 393, Macmillan, New York (1977). In Haseltine, that sensitizing dye is a methine dye. The excited dye injects an electron into the conduction band of the silver halide, which is trapped in the form of a metallic silver atom. *Id.* Applicants are unclear how this relates to the presently claimed method for determining the presence of an analyte of interest in a sample. Use of an agent that enhances silver halide pigment sensitization in a photograph is clearly not the same as a staining solution for the detection of analytes in a sample.

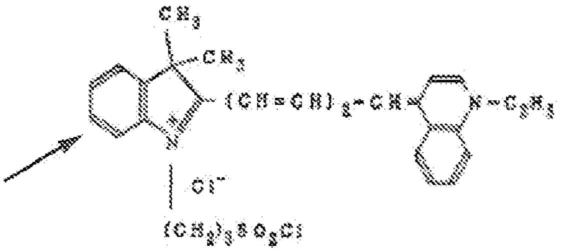
In order for a reference to anticipate a claim under 35 U.S.C. § 102, every element of the claim must be present in the cited reference. Since Haseltine fails to describe the methods and compounds of the present claims, Applicants respectfully request withdrawl of the rejection under 35 U.S.C. § 102(b).

Rejection Under 35 U.S.C. § 103(a)

II. Claims 1-4, 6, 9, 10, 13-17, 20, 21, 23-25, 38, 39 and 41-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katayose et al. (JP 05-287209). Applicants respectfully traverse this rejection because not all of the present claim limitations are taught or suggested by Katayose.

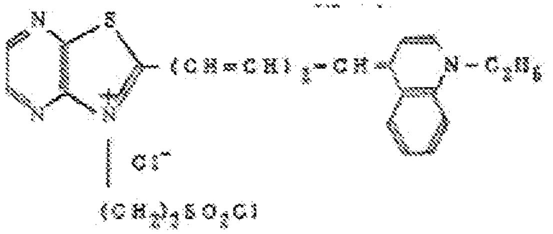
According to the Office Action, Katayose teaches the presently claimed method for determining the presence of an analyte in a sample utilizing dye compounds described therein, which are purportedly encompassed by the present claims. Applicants respectfully disagree.

Katayose describes functionalizing a nucleic acid primer with a reactive linker and conjugating compound 1 to the linker through compound 1's propylsulfonyl appendage (*see* Example 7, pages 8-9 of the translation of JP 05-287209). Compound 1 is an indolinium compound having the following structure:



The Examiner will note that the inolinium moiety contains a carbocyclic phenyl ring, indicated with an arrow, fused to the pyrrolinium moiety. Conversely, ring-A in the present claims requires that a nitrogen atom be present as one of the ring atoms.

Katayose does not teach a method for determining the presence of an analyte in a sample, as presently claimed, with a compound described by Formula I. Without any explicit teaching in Katayose, the Office Action apparently assumes that Compound 3 (Example 2) in Katayose is amenable to the same sort of reaction as Compound 1 through it's propylsulfonyl appendage:



, and that "forming a covalent bond between the dye and [known/synthetic] oligonucleotide primers" is equivalent to identifying an analyte in a sample by incubating the sample with a staining solution to form a dye analyte complex. The Examiner will note that the presently claimed staining solution comprising a compound of Formula I is capable of direct analyte detection, unlike Katayose, which provides a label for a pre-functionalized primer that can react after chemical modification.

Furthermore, even if detection of an analyte with Katayose's Compound 3 was possible, there remains a more fundamental issue: as amended, the only appendage permitted by the present claims at position R^2 is an unsubstituted alkyl group. The alkyl group is not amenable to nucleophilic attack by any linker or nucleic acid molecule described in Katayose. Accordingly, not only is Compound 3 in Katayose excluded by the present claims, the reactive (i.e. electrophilic) point of attachment for nucleic acid conjugation is also excluded. Without such a facet, the Katayose compounds are unable to bind the nucleic acids primers.

To support an obviousness rejection under 35 U.S.C. § 103, "all the claim limitations must be taught or suggested by the prior art." M.P.E.P. § 2143.03. Katayose fails to describe all of the limitations of the present claims. Furthermore, since any modification of Katayose's compounds leading toward the present claims is unsupported by the cited references and such a modification would in fact make Katayose's invention inoperable, it is respectfully submitted that the obviousness rejection is improper and should be withdrawn.

III. Claims 5, 11, 22, and 40 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Katayose in view of Mills et al. (U.S. Patent No. 5,221,518). As mentioned above, Katayose fails to describe the limitations of claims 1-4, 6, 9, 10, 13-17, 20, 21, 23-25, 38, 39 and 41-43 from which the presently rejected claims depend. Therefore, irrespective of Mills' alleged teaching of separation of sequencing reaction products using agarose or polyacrylamide gels, all of the elements of the claims have not been taught by the references. Accordingly, the obviousness rejection to 5, 11, 22, and 40 is improper and should be withdrawn.

IV. Claim 12 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Katayose in view of Leushner et al. (U.S. Patent No. 6,083,699). Applicants reiterate previous assertions that Katayose fails to teach or suggest the limitations of claims 1-4, 6, 9, 10, 13-17, 20, 21, 23-25, 38, 39 and 41-43. Leushner fails to cure the deficiencies in Katayose and therefore the obviousness rejection over claim 12 is improper and should be withdrawn.

CONCLUSION

In view of the enclosed amendments and remarks, it is respectfully submitted that this application is now ready for allowance. Early notice to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (541) 335-0165.

Respectfully submitted,

Date: 9/11/06

Joel S

Joel Silver
Reg. No. 53,866

Molecular Probes, Inc. (A wholly owned subsidiary of Invitrogen Corp.)
29851 Willow Creek Rd.
Eugene, Oregon, 97402
Phone: (541) 335-0165
Facsimile: (541) 335-0354